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TITLE: AN EPIGENETIC BIOMARKER IN PTSD

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14. ABSTRACT
There has been a growing recognition of the importance of epigenetic markers to PTSD. Epigenetic modifications are changes to the function (but not structure) of DNA that are caused by environmental exposures. To examine the extent to which an epigenetic marker – cytosine methylation of the human glucocorticoid receptor as measured on the lymphocyte – provides a relevant biomarker for PTSD. This will be accomplished by comparing cytosine methylation in combat veterans with and without PTSD. A second aim is to determine the association between cytosine methylation and the expression of glucocorticoid receptor related genes and splice variants of the human glucocorticoid receptor. Because we propose to measure cytosine methylation in the context of a large, multidisciplinary study (Biomarkers for PTSD: PI Dr. Charles Marmar NYUMC) we also propose to examine the relationship between this epigenetic measure and other well-studied correlates of PTSD.

15. SUBJECT TERMS
Post-traumatic Stress Disorder; Epigenetics; Gene Expression

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Final Report for Army Award W81XWH-09-1-0692, entitled "An Epigenetic Biomarker for PTSD"

INTRODUCTION:

There has been a growing recognition of the importance of epigenetic markers for PTSD.[1-2] There have also been recent developments in laboratory methodologies for examination of such markers in relevant human tissue.[1] Several recent findings not only implicate epigenetic mechanisms in PTSD, but are not well-explained by any other cause.[1-4] It has therefore become of great interest to develop and employ methodologies for examining epigenetic modifications in PTSD as these are likely to be central to understanding the interaction of risk and expression of the disorder. The present study seeks to supplement the parent 'Biomarkers for PTSD' study, also funded by the Department of Defense by assessing and identifying an epigenetic modification associated with PTSD vulnerability that is functionally related to PTSD expression in conjunction with the variety of other biomarkers that are being examined under the parent grant.

BODY:

This grant was used to develop and establish an epigenetic assay for use in OEF/OIF veterans that have been and will continue to be recruited through parent grant "Biomarkers for PTSD". No participants were recruited under this protocol, but the parent grant will remain open and all further study procedures will be housed under that protocol. An assay for examining DNA methylation of the GR gene was developed and run on 45 participants who completed participation in the parent grant. These assays will continue to be performed on all participants in the parent project and data gathered under this protocol will be subsumed under that project.

KEY RESEARCH ACCOMPLISHMENTS:

The following two abstracts will be presented at the annual ISTSS conference in November 2011:
"Evidence of Epigenetic Alterations in Holocaust Offspring"
"Using Epigenetic and Molecular Changes in PTSD as Therapeutic Target."
This third abstract will be presented at the annual ACNP conference in December 2011:
"Cytosine Methylation and Expression of GR related genes in association with PTSD treatment response."

REPORTABLE OUTCOMES:

The epigenetic assay that was developed for use in association with PTSD will be used in other populations recruited through the following protocols: including DOD-funded "Improving PTSD outcomes in OEF/OIF returnees: A randomized clinical trial of hydrocortisone augmentation of prolonged exposure therapy," as well as NIMH-funded "Identification of an Epigenetic Risk Marker for PTSD." Furthermore, this assay has been proposed for use in several pre-proposal grants, including "Administration of a single oral dose of prednisone in the Golden Hours as a potential secondary prevention in PTSD: A double-blind, prospective, placebo-controlled study" and "Efficacy of Yoga in treatment of PTSD in Warfighters."

CONCLUSION:

The epigenetic assay outlined in the original grant was successfully developed on run on samples from 45 participants recruited through the parent grant "Biomarkers for PTSD." This assay will continue to be run on all of the other participants recruited through the parent grant, as well as several other existing grants, and has been suggested in several grant proposals currently under review. There have been no publications to date, although there are plans to submit manuscripts within the next 12 months.

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[3] Oberlander TF, Weinberg J, Papsdorf M, Grunau R, Misri S, Devlin AM. Prenatal exposure to maternal depression, neonatal methylation of human glucocorticoid receptor gene (NR3C1) and infant cortisol stress responses. Epigenetics. 2008 Mar-Apr;3(2):97-106.

[4] Charuvastra A, Cloitre M. Social bonds and posttraumatic stress disorder. Annu Rev Psychol. 2008;59:301-28. Review.